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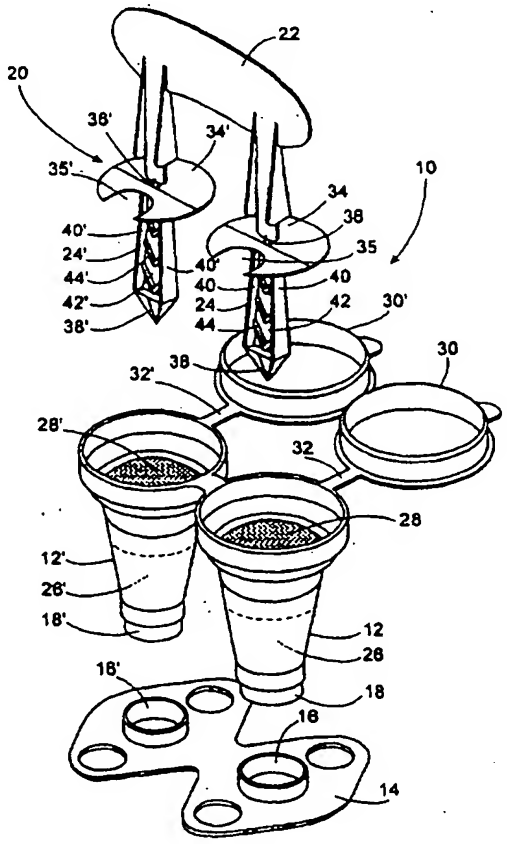
(54) Title: COLLECTION AND TRANSPORTATION OF A PASTY MATERIAL SAMPLE

(57) Abstract

A system for collecting, storing and transporting of specimens of a pasty material, e.g. stool is provided. The system comprises at least one container holding a preservation medium for preserving a chemical entity or living matter to be assayed in a specimen, the container being sealed by a pierceable membrane having a closure arrangement for sealing the container after the membrane is pierced. The system further comprises a sampling device having a handle and at least one elongated specimen collecting member detachably attached thereto, the collecting member being adapted to be received within the container and having the pasty material retaining portion and a piercing tip for piercing the membrane at a lowermost end thereof remote from said handle, for piercing said film. Also provided is a stool collecting device for easy collecting of excreted stool.



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COLLECTION AND TRANSPORTATION OF A PASTY MATERIAL SAMPLE

FIELD OF THE INVENTION

The present invention concerns a system for the collection and transportation of a pasty material sample, for example of stool, which is to be distributed in a transport and/or suspension medium.

BACKGROUND OF THE INVENTION

Collection and transportation of a pasty material, such a stool, food samples, soil samples and the like for the purpose of laboratory manipulation such as detection of microorganism being bacteria or parasites, detection of cryptic blood, preparation of a biochemical profile, etc., is an essential component of modern medicine, health care and environmental management.

Often, when the pasty material is transported to the laboratory without a preservation medium, by the time it reaches a laboratory no viable micro-organisms can be detected, and the result of the laboratory tests are thus distorted.

In order to overcome this problem, various devices and systems for the collection and transportation of pasty material have been developed, in which the pasty material is distributed in a medium capable of maintaining viable microorganisms. Usually, such devices comprise a container holding the medium, and a sampler capable of picking up a small portion of the pasty material and placing it within said container.

US 5,149,506 discloses a device for collection and transportation of a stool sample which is composed of a container with a lid having a spoon secured to the underside of the lid, the container being filled with a liquid capable of maintaining microorganisms in a viable form.

US 4,559,839 discloses a stool collection and concentration receiver comprising a container holding a medium and including within it a collecting-filtering device comprising a stick for picking up the stool sample and sieve through which the diluted stool is filtered.

US 4,678,559 discloses a sampling vessel for pasty sample material comprising a sample-taking cup fitted on the lid of a container and facing towards the container's bottom.

In the above three patents the sampling member, used to pick the sample of the pasty material, is held *a priori* within the container holding also the preservation medium. This feature has the following problems:

- in order to sample the pasty material the container holding both the medium and the sampling member has to be opened, thus increasing the chances of contamination of the sterile medium by ambient atmosphere, or by the hands of the user and increases the possibility of spillage due to mishandling;
- once the sampling member is taken out of the medium filled container it may drip the medium on to its surrounding, and where the medium contains harmful ingredients, e.g. formaldehyde or mercury which are present in some preservation media, this may cause some damage if it comes into contact with the user's skin or eyes;
- the wet sampling member, once coming into contact with the pasty material sample, adds to the sample also a certain amount of the transport or suspension medium itself. This may be problematic if another sample of the pasty material is to be transferred into another container holding a different medium, since the second sample may already be contaminated by the first medium.

A stool sample is typically subjected to two different tests one being a bacteriological test and the other a parasitological test. The medium

required to maintain viable bacteria and the medium required to maintain viable parasites are not only different but are mutually exclusive, i.e. one type of medium damages the other type of microorganism. Thus, in the case of a pasty material which is to be sampled for the purpose of two or more different laboratory assay, such as stool, it would be preferable to provide a system for collection and transportation of pasty material which comprises two or more separate containers each one holding a different transport or suspension medium.

Finally, the above-mentioned prior art devices for collection and transportation of stool, do not address the problem of obtaining the original stool sample in a convenient manner which enables easy access to the user and the prior art tends to leave the solution to the problem to the skills of each user.

The present invention intends to provide an answer to some of the above-noted problems.

GENERAL DESCRIPTION OF THE INVENTION

The present invention provides a system for collecting, storing and transporting of specimens of a pasty material, comprising:

at least one container holding a preservation medium for preserving a chemical entity or living matter to be assayed in the specimen, the container being sealed by a pierceable membrane and having a closure arrangement for sealing the container after the membrane is pierced; and

a sampling device having a handle and at least one elongated specimen collecting member detachably attached thereto, the collecting member being adapted to be received within the container and having a pasty material retaining portion and a piercing tip for piercing the membrane at a lowermost end thereof remote from said handle, for piercing said film.

The system of the present invention is suitable for collecting, storing and transporting of any pasty material, for example, stools, food samples, e.g. soft cheese, yogurt, various spreads; soil samples, e.g. mud samples; and many others. With appropriate preservation media, the

samples may be stored for a lengthy period of time prior to assaying for the chemical entity or living matter. The composition of the medium depends on the type of entity which should be preserved and subsequently assayed: for example, if the entity is a chemical substance, the medium will have a composition which ensure that the substance is preserved in a manner to avoid its deterioration; if the assayed entity is microorganism or any other living matter, the medium will be designed so as to maintain such microorganisms or other living matter in a viable condition. A system for collecting, storing and transporting specimens to subsequent assays for living matter, e.g. microorganisms, yeasts or parasites thereon, is a preferred embodiment of the invention. In accordance with a particularly preferred embodiment, the pasty material is stool.

At times a variety of different entities have to be assayed in the pasty material. This is the case, for example, in stool, where it is generally desired to assay both bacteria and parasites, which as noted above, require different media. A system for assaying a plurality of entities, which require different media, comprises at least two containers, each holding a different preservation medium, each suitable for different entities. The containers in such a system may be permanently attached to one another; or alternatively, the attachment of the two containers to one another being in a detachable fashion to allow detachment when the containers with the sample reaches the laboratory.

The closure arrangement is typically a rigid lid member attached to the container through a flexible linker.

The system further comprises a sampling device which is an element distinct and separate from the container. The provision of the container and a separate sampling device ensures that until the pasty material sample is introduced into the container, the medium therein is kept totally sterile. As already noted above, in prior art devices, where a sampling device was stored within the container, it was necessary to open the container prior to sampling, with an inevitable loss of sterility.

The sampling device comprises a handle which is detachably connected to the at least one collecting member. The detachable connection can be by a breakable portion, by a fastener capable of holding or releasing an attachment element in the collecting member, etc. The at least one collecting member is adapted to be received within corresponding at least one container. (It will be appreciated, that the number of collecting members will typically correspond to the number of containers, and where the containers are held together, the spacing between the collecting members will be made to correspond to the distance between the container such that all collecting members may be inserted simultaneously to the respective containers).

Each collecting member has a piercing tip for piercing the container's pierceable membrane and has a pasty material retaining portion. Once the membrane is pierced by the piercing tip, the collecting member is pushed down until the material retaining portion is accommodated within the container and embedded in the medium. Then, the handle is detached from the collecting member. As will be appreciated, there are a number of different constructions which have the capability of retaining a specimen of the pasty material: for example, a rough surface having multiple depressions and/or protrusions; a helical structure; a ladder-like shaped structure having straight, curved or V-shaped ribs; a structure comprising a planar stem with protrusions, which may have the form of straight, curved or V-shaped ribs, or which may comprise a plurality of bulges, etc.

In order to ensure that the pasty material will be retained on the retaining portion and will not be smeared on the membrane, it is preferable that the pasty material retaining portion has the widest cross-section at the lowermost part, near the piercing tip. This will ensure that the hole in the membrane which will be made by the piercing tip, will be sufficiently large to ensure free passage of the remaining portions of the collecting member. In accordance with an embodiment of the invention, the pasty material retaining portion is defined by two lateral side walls which are wider than the pasty material retaining portion. Thus during insertion, only these side

walls come into contact with the membrane, whereby the majority of the specimen of the pasty material does not come into contact with the membrane.

In accordance with a preferred embodiment of the invention, the sampling device comprises an integral disc with its surface being essentially perpendicular to the longitudinal axis of the collecting member. The shape of the disc is such that once the collecting member is introduced into the container, the disc is snugly retained within the inner walls of the container thus stabilizing the position of the collecting member within the container. The disc preferably defines an opening which allows the insertion of a laboratory sampling device, e.g. a pipette, a sampling needle, etc, for withdrawing a portion of the specimen, this without a need to remove the collecting member with the integral disc.

As can be seen, the system of the invention minimize possible contact between a sample and a laboratory technician, which is especially important in cases where the sample may contain hazardous materials or microorganisms.

In accordance with a preferred embodiment of the invention, as already noted above, the pasty material is stool. In accordance with this embodiment, the system may comprise a stool collecting device, which has a collecting member for collecting an excreted stool sample and attachment members for attachment to a toilet seat. The stool collecting device also forms an independent aspect of the invention. The device is typically made of a sheet, e.g. a paper sheet, with the collecting portion and the attachment member being integral, i.e. made of the same sheet. The attachment member may be a sheet portion adapted for wrapping around a toilet seat and are then retained by virtue of being sandwiched between the toilet seat and the upper edges of the toilet bowl. Alternatively, the attachment member may comprise adhesive patches on a bottom face of the attachment member for adherence therethrough to the toilet seat. The adhesive patches are *a priori* protected with the protection being used prior to use and attachment thereof to the toilet seat.

In accordance with an embodiment of the invention, the stool collecting member is a sheet portion suspended between the attachment members. Alternatively, the stool collecting member may have the form of a sack for collecting excreted stool sample. Such a sack may be provided with openings at its bottom to allow a drainage of excreted fluid while retaining the stool.

The stool collecting device is preferably made of a flushable material, e.g. thin paper, and after use may be dropped into the toilet bowl to be flushed thereby.

The invention will now be further illustrated by the following description of a specific embodiment and by the annexed drawings. The illustrated embodiment concerns a system for collecting, storing and transporting stool samples. However, as will no doubt be appreciated by the artisan, this is an example only and the invention pertains also to systems for collecting specimens of pasty material other than a stool.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 is an exploded view of a system of the invention comprising two containers and a sampling device with two corresponding collecting members;

Fig. 2 shows the system, with the containers being assembled on a base and with the collecting member holding a stool sample;

Fig. 3 shows the system after combining the sampling device with the containers with the collecting member being inserted in the container;

Fig. 4 shows the system after separating between the handle and the collecting members;

Fig. 5 shows the system after closing of the lid, ready for transportation into the laboratory;

Fig. 6 shows a stool collecting device in accordance with the invention;

Figs. 7 and **8** show stool collecting devices in accordance with other embodiments of the invention, attached to a toilet seat.

DESCRIPTION OF SPECIFIC EMBODIMENTS

Reference is first being made to Fig. 1, which is an exploded view showing the various components of the system, generally designated 10. The system 10 comprises two attached containers 12 and 12', a base member 14 with two receptacles 16 and 16' adapted to receive the bottom ends 18 and 18' of containers 12 and 12'; the system further comprises a sampling device 20 having a handle 22 and two collecting members 24 and 24'.

Containers 12 and 12' hold respective media 26 and 26', which may both be the same, but are typically different, e.g. one being a media for preserving bacteria and the other for parasites. Media 26 and 26' are typically semi-solid media, e.g. agar-based, but may also be a lipid, e.g. a culture media. Media 26 and 26' are contained in a portion of the containers sealed by pierceable membranes 28 and 28', the membranes being made of aluminum foil, a laminate of an aluminum foil and a plastic, (e.g. polyethylene) film, etc. Containers 12 and 12' are provided with respective lids 30 and 30' which are linked to the containers by means of linkers 32 and 32'. Sampling device 20 has integral disc members 34 and 34' at the upper end of specimen collecting members 24 and 24'. Disc 34 and 34' have each respective openings 35 and 35', the functions of which will be explained further below. Handle 22 is connected to disc members 34 and 34' by means of breakable neck portions 36 and 36' by small lateral respective movements of the handle and the collecting members connecting necks 36 and 36' break whereby handle 22 and collecting members 24 and 24' are separated.

Collecting members 24 and 24' are elongated and have each a piercing tip 38 and 38' at its bottom end adapted for piercing membranes 28 and 28'. Collecting members 24 and 24' have two lateral walls 40 and 40' which define the stool retaining portion consisting also of planar members 42 and 42' disposed within the lateral walls and carrying a plurality of V-shaped protrusions 44 and 44'. As can be seen, the collecting members

have the largest cross-section at a portion adjacent piercing tips 38 and 38' thus the hole which is created in the membranes 28 and 28' allows easy passage therethrough for the remaining portions of the collecting members. Furthermore, lateral walls 40 and 40' ensure that the stool specimen held on planar members 42 and 42' is not removed by the membranes 28 and 28' during passage of collecting members 24 and 24'.

In order to collect specimens of pasty material, collecting members 24 and 24' are inserted into a sample of the pasty material, e.g. stool, and thereby specimens are retained on collecting members 24 and 24'. Sampling device 20 with stool specimens 50 and 50' retained on collecting members 24 and 24' is seen in Fig. 2. Also seen in this figure are containers 12 and 12' assembled on base member 14.

After collection of the specimens, the sampling device and the containers are combined by first pressing piercing tips 38 and 38' against membranes 28 and 28' and then pushing the collecting members until they are accommodated within containers 12 and 12' with the collecting members being embedded within the medium containing the containers. Fig. 3 shows the sampling device 20 and containers 12 and 12' immediately after combining the two. As can be seen, the size of disc members 34 and 34' are such that they are accommodated snugly within the inner walls of the container stabilizing the collecting member in position.

At a next step shown in Fig. 4, the handle 22 is moved naturally thus breaking necks 36 and 36' leaving the collecting members within containers 12 and 12'. At a next step shown in Fig. 5, lids 30 and 30' are used to close containers 12 and 12' and at this state the containers are shipped to the laboratory. In the laboratory, the lids are opened to a state similar to that shown in Fig. 4, and then a sampling device, e.g. a pipette, a bacteriologic needle, etc., is inserted through openings 35 and 35'. Thus, sampling of the specimen for laboratory testing does not require removal of the collecting member, as in the case of prior art devices.

A stool collecting device in accordance with an embodiment of the invention is shown in Fig. 6. The device, generally designated **60** is made of a sheet, e.g. paper, particularly thin paper which is flushable in a toilet. The device has a central collecting member, which is a portion of a sheet having the form of a sack, and has two attachment members **64** and **66** which are of a length such that their ends will reach two opposite sides of a toilet seat. The attachment members **64** and **66** have two adhesive patches **68** and **70**, on bottom faces of the device. Adhesive patches **68** and **70** are *a priori* covered by a protective cover (now shown) and prior to use, the cover is removed and then these patches can adhere to the toilet seat. The device is fixed such that stool excreted by a person sitting on the toilet, falls into a sack-like collecting member **62** for later sampling by the sampling device. As can further be seen in Fig. 6, collecting member has at its bottom four openings **72** which are intended to allow a discharge of fluids which may be excreted together with the stool.

Two other embodiments of a stool collecting device are shown in Figs. 7 and 8, fixed to a toilet seat. The stool collecting device **80** shown in Fig. 7, is in principle similar to device **60** shown in Fig. 6 in that it comprises a central sack-like portion **82** and peripheral attachment flaps **84** and **86**. Device **80** is fixed to a toilet seat **88** by means of adhesive patches, similarly as in the case of device **60** in Fig. 6.

Device **90** shown in Fig. 8, comprises a stool collecting portion **92** which is a sheet, e.g. made of paper, suspended between two attachment members **94** and **96** which are two flaps which are wrapped around two opposite sides of the toilet seat **98**, and are fixed by virtue of being clamped between the toilet seat and the underlying toilet bowl (not shown). In addition a device of this embodiment may also comprise adhesive patches at the bottom face members of **94** and **96** to aid in fixing them to the toilet seat.

Having now finalized the description of the specific embodiment, the artisan will no doubt appreciate that the above specific embodiment is

an example only and a myriad of other designs of the container and the sample device as well as the stool collecting device are possible, all being within the scope of the invention as defined in the appended claims.

CLAIMS:

1. A system for collecting, storing and transporting of specimens of a pasty material, comprising:

at least one container holding a preservation medium for preserving a chemical entity or living matter to be assayed in the specimen, the container being sealed by a pierceable membrane and having a closure arrangement for sealing the container after the membrane is pierced; and

a sampling device having a handle and at least one elongated specimen collecting member detachably attached thereto, the collecting member being adapted to be received within the container and having a pasty material retaining portion and a piercing tip for piercing the membrane at a lowermost end thereof remote from said handle, for piercing said film.

2. A system according to Claim 1, wherein the medium is of a kind which maintains living matter in a viable condition.

3. A system according to Claim 2, wherein the pasty material is stool.

4. A system according to Claim 1, comprising two containers, one holding a medium for bacteria and another for holding a medium for parasites.

5. A system according to Claim 4, wherein the two containers are attached to one another.

6. A system according to Claim 4 or 5, wherein the sampling device comprises two specimen collecting members.

7. A system according to any one of the preceding claims, wherein said collecting member has a piercing tip for piercing the containers' pierceable membrane and has a pasty material retaining portion.

8. A system according to Claim 7, wherein the pasty material retaining portion has the widest cross-section at a lowermost part thereof, near the piercing tip.

9. A system according to any one of the preceding claims, wherein the sampling device comprises an integral disc in an upper end of the collecting member, with its surface being essentially perpendicular to the longitudinal axis of the collecting member.

10. A system according to Claim 9, wherein the shape of the disc is such that once the collecting member is introduced into the container, the disc is snugly retained within the inner walls of the container.

11. A system according to Claim 10, wherein the disc defines an opening which once the collecting member is placed within the container, allows insertion of a laboratory sampling device into the medium, without a need to remove the collecting member.

12. A stool collecting device which has a collecting member for collecting an excreted stool sample and attachment members for attachment to a toilet seat.

13. A device according to Claim 11, made of a sheet with a stool collecting portion and integral flats for attachment to a toilet seat.

14. A device according to Claim 12, comprising adhesive patches for fixing the device into a toilet seat.

15. A system according to any one of Claims 1-10, comprising a stool collecting device according to any one of Claims 11-13.

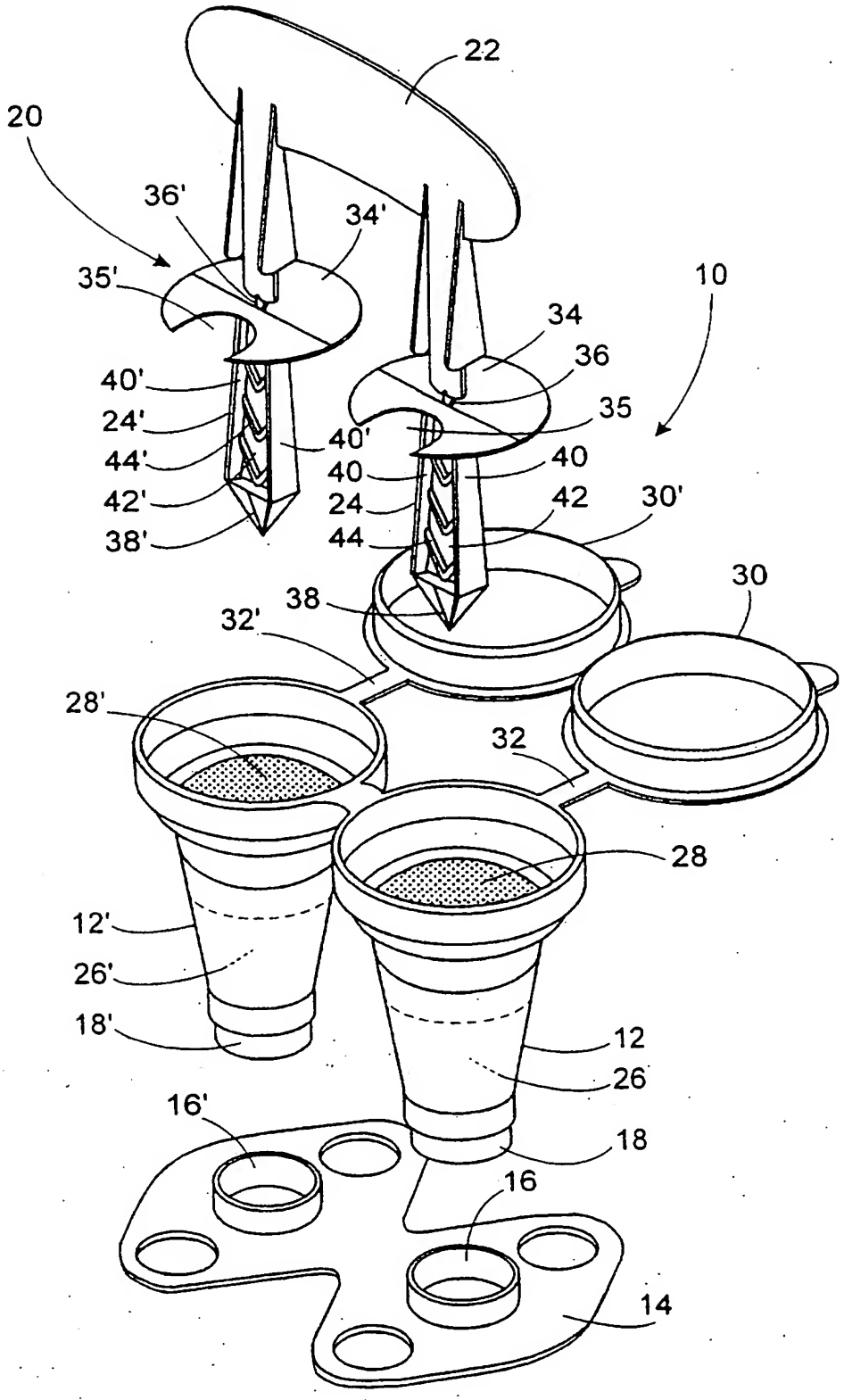
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Fig. 1

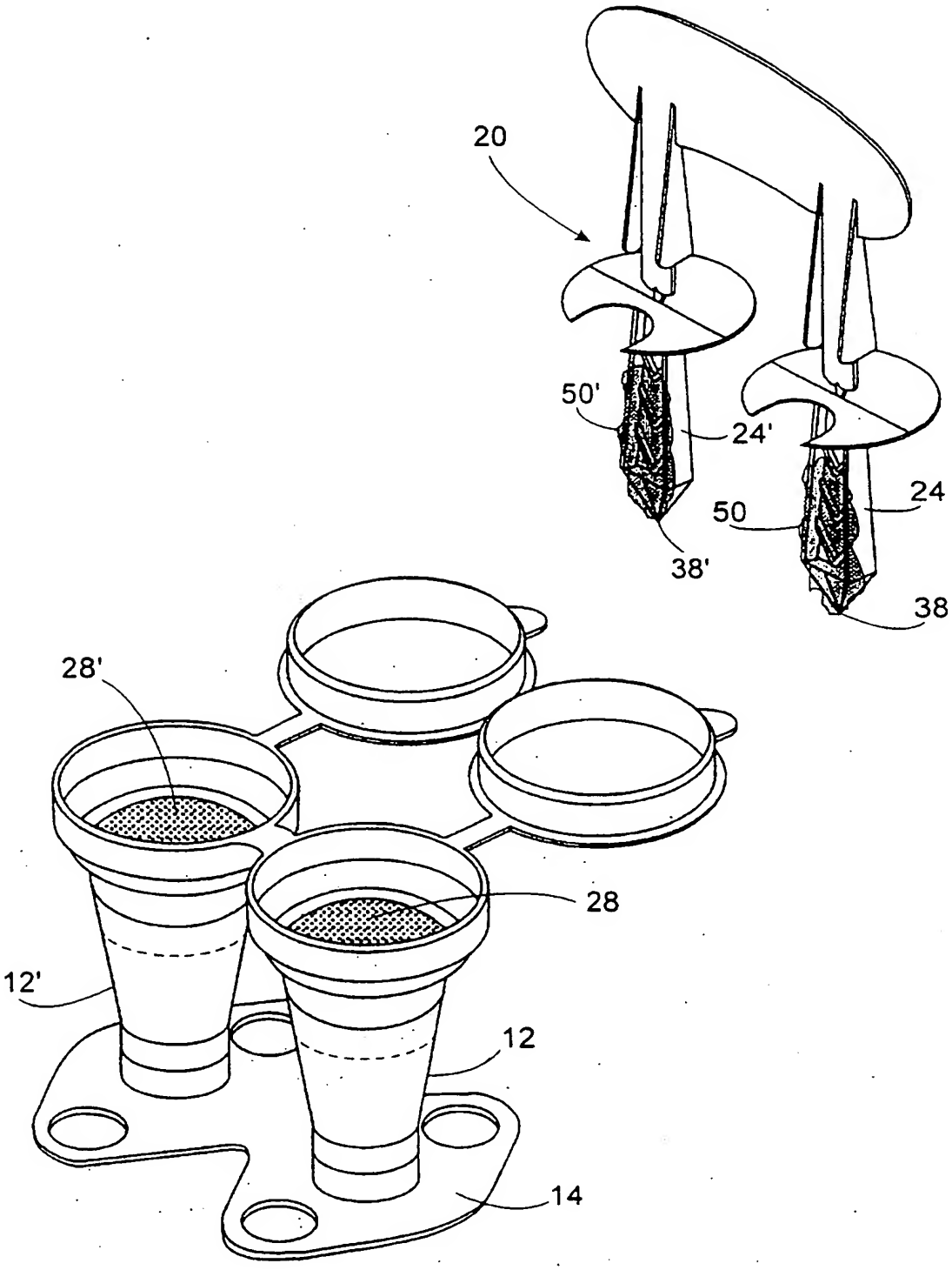

Fig. 2

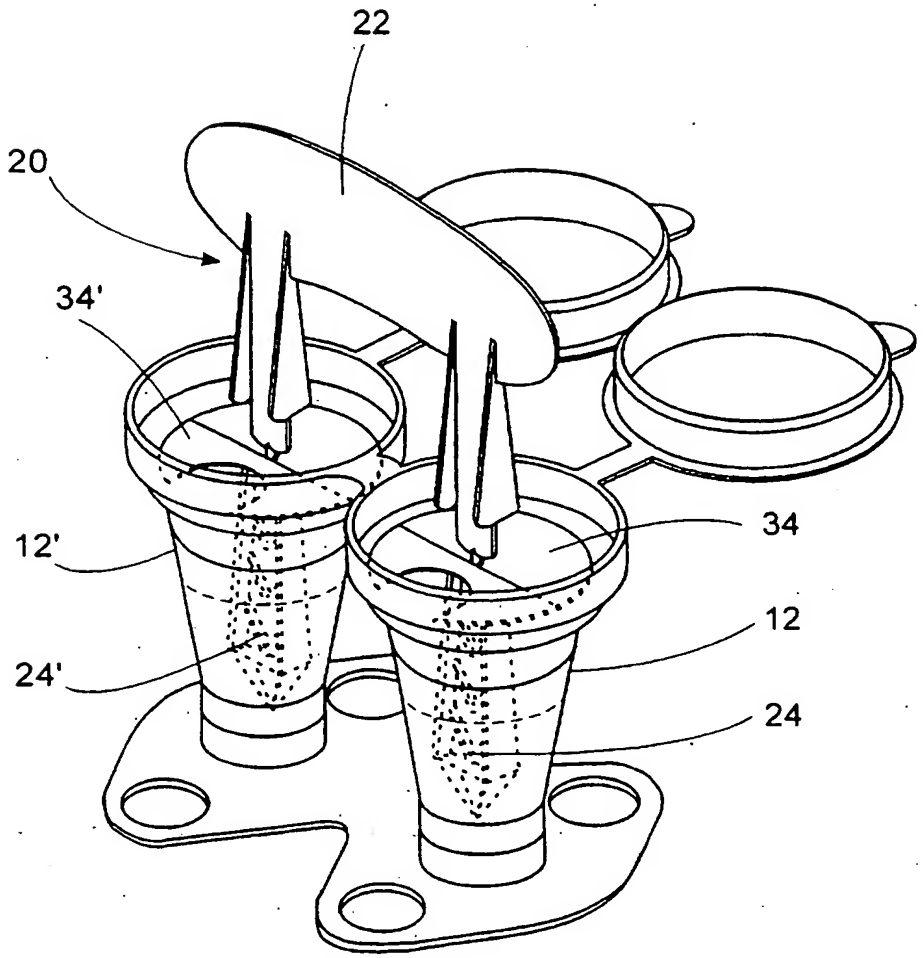

Fig. 3

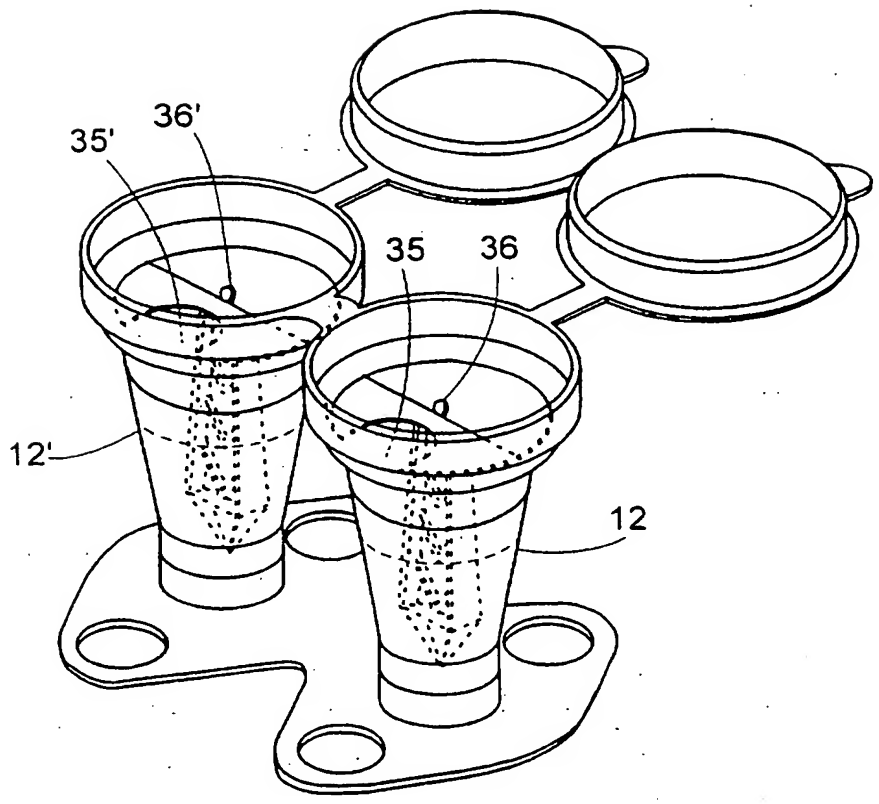

Fig. 4

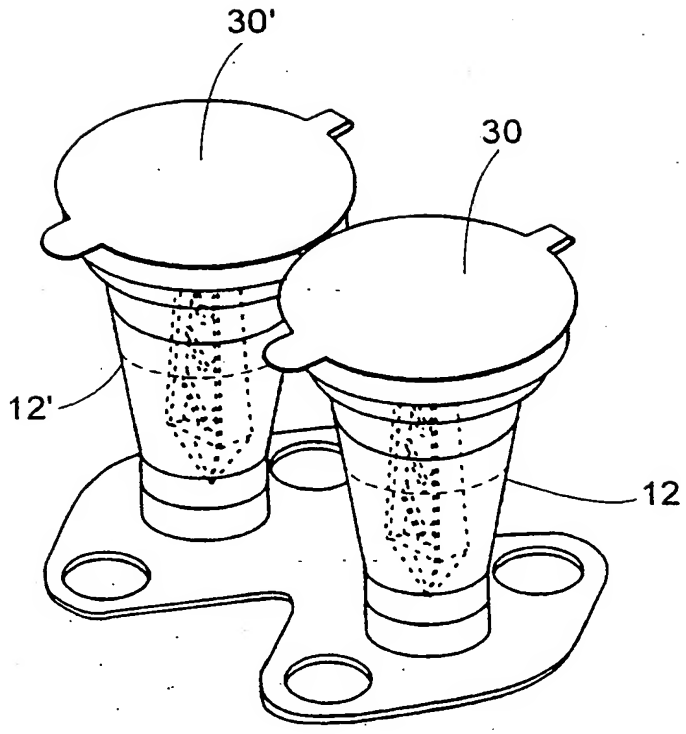

Fig. 5

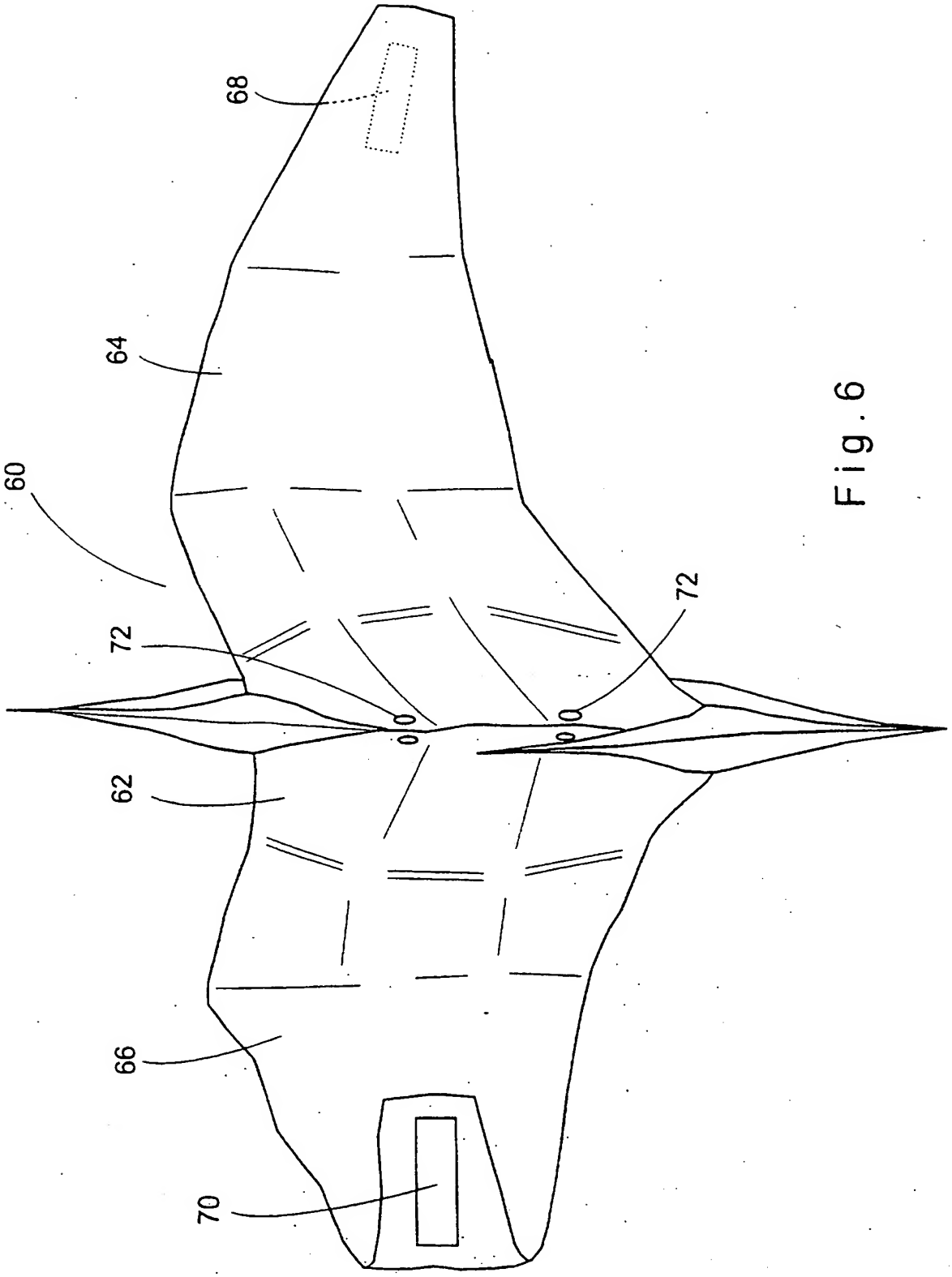

Fig.6

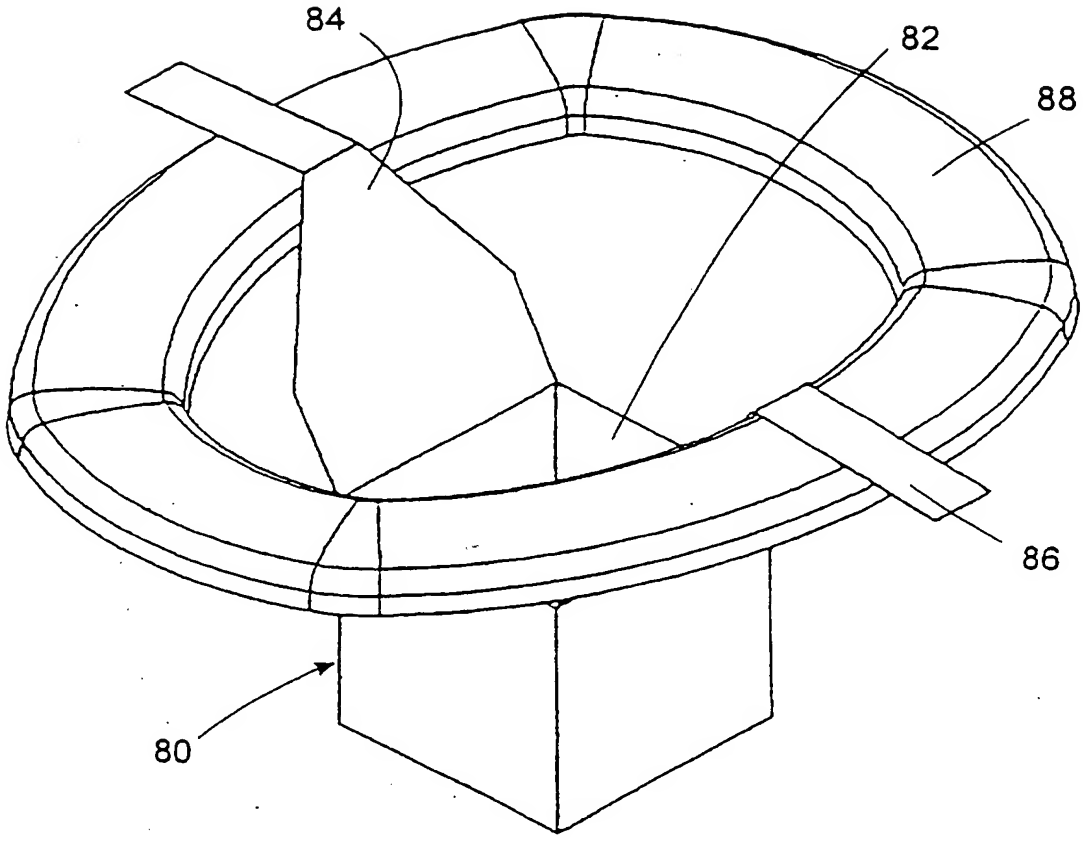

Fig. 7

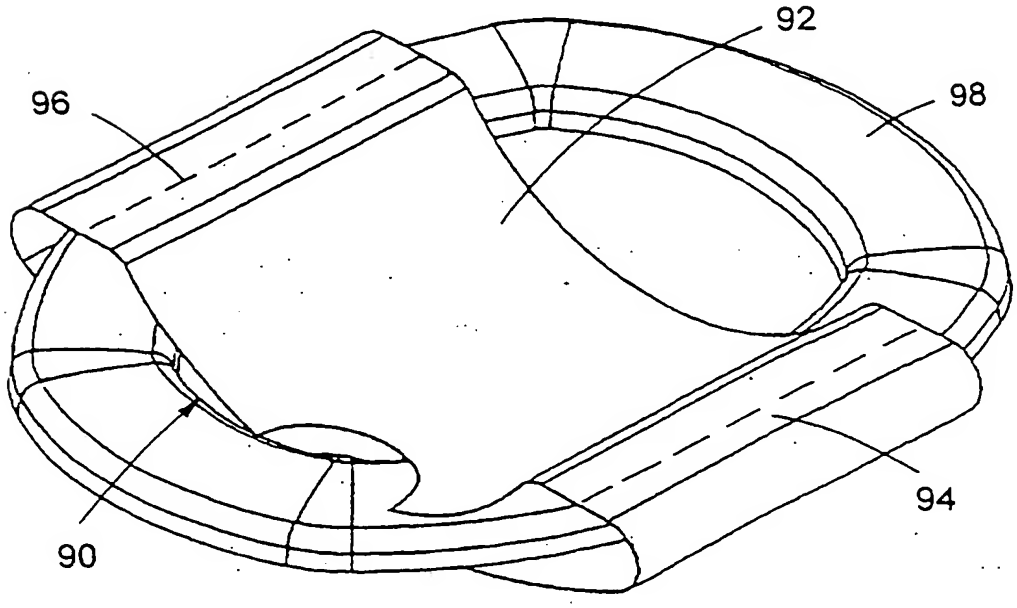

Fig. 8

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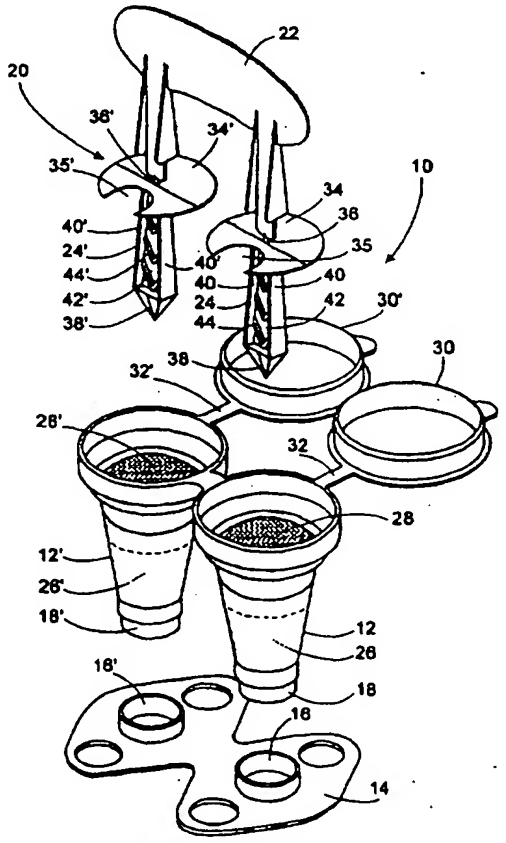
(54) Title: COLLECTION AND TRANSPORTATION OF A PASTY MATERIAL SAMPLE

(57) Abstract

A system for collecting, storing and transporting of specimens of a pasty material, e.g. stool is provided. The system comprises at least one container holding a preservation medium for preserving a chemical entity or living matter to be assayed in a specimen, the container being sealed by a pierceable membrane having a closure arrangement for sealing the container after the membrane is pierced. The system further comprises a sampling device having a handle and at least one elongated specimen collecting member detachably attached thereto, the collecting member being adapted to be received within the container and having the pasty material retaining portion and a piercing tip for piercing the membrane at a lowermost end thereof remote from said handle, for piercing said film. Also provided is a stool collecting device for easy collecting of excreted stool.



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INTERNATIONAL SEARCH REPORT

Intern. .nal Application No
PCT/IL 97/00017

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61B10/00 B01L3/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61B B01L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 93 09431 A (UNIV BIRMINGHAM) 13 May 1993 see page 9, line 16 - page 11, line 23 ---	1,3,7
A	PATENT ABSTRACTS OF JAPAN vol. 018, no. 092 (P-1693), 15 February 1994 & JP 05 296997 A (MEIJI SEIKA KAISHA LTD;OTHERS: 01), 12 November 1993, see abstract -----	1-3

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
23 May 1997	1 8 08. 97

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+ 31-70) 340-2040, Tx. 31 651 epo nl, Fax (+ 31-70) 340-3016	VERELST P.E.J.

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

I. national application No.
PCT/IL 97/00017

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. Subject: Claims 1-11 container for collecting storing and transporting
2. Subject: Claims 12-15 device for stool collecting

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1. Subject: Claims 1-11

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inter. ..nal Application No
PCT/IL 97/00017

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9309431 A	13-05-93	AU 665376 B	04-01-96
		AU 2801292 A	07-06-93
		CA 2122597 A	13-05-93
		DE 69219612 D	12-06-97
		EP 0610325 A	17-08-94

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Apparatus for the collection and recovery of saliva for use in diagnostic assays

Abstract

A device (50) for the recovery of saliva from an absorbent, compressible saliva collection device comprises a receptacle (51) and means (56) for compressing the saliva collection device when inserted therein to express saliva and entrained organic material, such as immunoglobulin, therefrom. The saliva collection device is suitably a mass of saliva absorbing fibrous material, such as rayon, having substantially no binding affinity for the organic material contained in the saliva. Expressed saliva is dispensed through an integral dropper mechanism (53) for use in an immunoassay.

(Fig. 6)

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1 APPLICATION No.....

Apparatus for the collection and recovery of saliva for use in diagnostic assays

This invention relates to apparatus for the collection and recovery of saliva for use in diagnostic assays.

Diagnosis of a disease state in a subject frequently requires testing of a body fluid or tissue. Blood or a blood fraction is currently the body fluid which is the basis of the majority of diagnostic testing. However, blood collection is an invasive technique which can be hazardous.

Diagnostic tests which provide rapid responses and utilise simple, non-invasive technologies have become increasingly accepted because of their reliability, ease of use and convenience. For example, the majority of pregnancy testing is currently carried out by rapid, immunoassay-based tests using urine. Chemical dipstick tests for the detection of various substances in urine have been routinely used in hospitals, clinics, doctors' surgeries and homes for several years.

Increasing concerns with the risk of obtaining blood samples through routine blood sampling (venipuncture), in particular because of the fear of accidental contraction of the Human Immunodeficiency Virus (HIV) and ultimately full blown Acquired Immunodeficiency Syndrome (AIDS) and hepatitis, have resulted in the need to replace blood testing with non-invasive test methods which can provide equally accurate results. The risks of accidental AIDS infection by healthcare professionals, the fear of the general public of contracting infection from healthcare professionals, and concerns of both groups over the disposal of blood contaminated waste should favour the use of non-blood based diagnostic tests.

It is estimated that AIDS will kill more than twenty million people worldwide by the year 2000 according to the United Nations Development Programme. The World Health Organisation (WHO) indicates that from nine to eleven million adults and one million infants

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A61B 10/00

worldwide have become infected with HIV and that a significant number remain undiagnosed. Heterosexual transmissions now account for over 90% of the new cases of HIV infections worldwide. WHO estimates that the number of HIV infections will at least triple and possibly quadruple in the next eight years.

Screening and diagnostic tests for the detection of infectious diseases and other purposes have traditionally used blood and blood fractions, such as serum. Such use of blood in infectious disease diagnostics originated when the technologies were less sensitive than they are now, and required a relatively high concentration of antibodies present in serum. More recent technology, including enzyme-linked immunosorbent assays (commonly referred to as ELISAs), has greatly increased the sensitivity and specificity of immunological methods, allowing for better detection of very small quantities of antibody in solution.

The increased sensitivity of the diagnostic tests means that other body fluids, such as saliva and urine, can also be used in the diagnosis of many diseases or conditions. Furthermore, saliva has significantly fewer proteins than blood, potentially increasing the specificity of saliva-based tests and reducing the number of false positive results. Recent medical studies have determined that antibodies to HIV can be found in mucosal transudate, which is the antibody carrying component of saliva. This relationship is analogous to the relationship of blood serum to whole blood.

The oral immune system interacts actively with the immune system of the rest of the body. Within the oral cavity there is found a specific site of antigen-antibody response which involves extraoral lymph nodes and intraoral lymphoid aggregations.

By saliva herein is included gingival liquid, hereinafter referred to collectively as saliva.

Saliva contains a complex mixture of inorganic and organic substances: these can be broadly subdivided into electrolytes, hormones, enzymes, proteins, low molecular weight compounds and vitamins.

The intraoral lymphoid tissue comprises essentially four distinct tissue aggregations: the gingival lymphoid tissue; salivary gland lymphoid tissue; scattered sub-mucosal lymphoid aggregations; and the tonsils.

The tonsils produce B and T cells. The predominant antibody formed by the tonsils is IgG. The tonsils also produce IgA, IgE and IgM antibodies in smaller amounts.

The salivary glands produce and secrete through their plasma cells predominantly IgA. The IgA antibodies produced by the salivary glands are referred to as the secretory IgA and they represent the major immunoglobulin fraction contained in saliva.

It is found that although IgA is the predominant Ig class present in saliva, viral-specific IgG and IgM is reliably detectable in infected individuals.

The gingival lymphoid tissue also contains plasma cells which are located generally near the blood vessels and produce IgG and very little IgA. It has been shown that the IgG secreted by the gingival lymphoid tissue is directly related to the IgG found in the blood.

The presence of IgG and secretory IgA in the saliva prompted the use of saliva as a basis for immunological assays. The suitability of saliva as a diagnostic body fluid has not been demonstrated for all diseases or even a significant proportion thereof. Recent studies have demonstrated that saliva can be successfully used in testing for various conditions and diseases, including HIV antibody detection, rubella and hepatitis.

If one is to successfully use saliva as a diagnostic body fluid, several key factors must be taken into consideration: a) the type of antibody to be detected or determined; b) assay sensitivity; and c) the method of saliva collection.

As indicated above, IgA antibodies are the major immunological fraction contained in saliva. In many instances, there are not enough specific IgA antibodies in saliva to perform a specific diagnostic test. Furthermore, the specific IgA may not be present in a sufficient amount to perform a test that compares favourably with a corresponding blood test. An example of the latter is the case of HIV1 antibodies.

It is known that saliva contains about 0.01-0.1% of the immunoglobulins contained in the blood. Because of the reduced immunoglobulin content of saliva relative to blood, it is necessary to use more sensitive antigen-antibody assay methods relative to corresponding assays performed on the blood or blood fractions.

The collection of saliva is a relatively complicated procedure and can lead to misleading results when the saliva is collected from the salivary glands because of the relatively small volumes that can be collected and because of the viscosity and high mucous content of saliva. Most of the methods currently employed involve collecting saliva through capillary tubes, suctioning into micro-pipettes or syringes. The use of saliva collected by the latter methods has inherent problems because of the high content of mucous and the limitations presented by the predominance of IgA, which is known not to be present in a sufficient amount in the case of certain specific antibodies.

In recent years much attention has been directed to the use of saliva for diagnostic purposes and new methods of saliva collection have been developed to collect IgG antibodies. Many of the new methods involve the absorption of saliva in the mouth by an absorbent material from which the collected saliva is extracted and processed. With such methods a number of potential problem areas arise: i) the

volume of sample collected; ii) the manipulation of the collected sample; iii) the mucous and tissue content of the collected sample; iv) the separation of the immunoglobulins from the mucous, tissue and saliva; v) the preservation or non-preservation of the immunoglobulins; vi) patient comfort during collection; and vii) the type of immunoglobulins collected.

One major advantage of the use of saliva as a body fluid for diagnostic assays is that the taking of saliva samples is non-invasive as compared with the taking of blood samples. Thus, the collection of saliva for such assays can be carried out in situations where the availability of syringes might be limited or where strict hygiene practices might not be adhered to.

We have found that absorbent materials currently used to collect saliva are usually cotton-based or based on other natural fibres such as paper and sponge and have a high affinity for organic substances contained in saliva, in particular, protein material and especially immunoglobulin, which is the most usual analyte targeted for diagnostic purposes. Because of this high binding, the saliva once collected must be treated chemically to release the analyte of interest. Such a treatment can affect the sensitivity and specificity of a diagnostic assay for the analyte.

Thus, in a study carried out by Chamnanpunt, J. and Phanuphak, P. of the Thai Red Cross Programme on AIDS, Bangkok, Thailand in which they evaluated a saliva collection device sold under the Trade Mark OMNISAL (Saliva Diagnostic Systems) and found that it had no advantages relative to simple spitting. The aim of the study carried out was to determine whether the collection device is better than simple saliva spitting in improving the sensitivity and specificity of the tests or in preserving the anti-HIV activity in the collected saliva. Chamnanpunt, J. and Phanuphak, P. found that compared to simple spitting, the saliva collection device had no benefit in increasing sensitivity of salivary anti-HIV testing or in preserving stored saliva.

Thus, there is a need for a saliva collection device which can be used to collect saliva in a sufficient volume to allow for the detection of an analyte of interest, while at the same time readily releasing the analyte when required, especially without the use of chemical releasing agents.

The use of saliva as a basis for diagnostic assays is desirable. However, the processing of saliva once collected currently involves the use of laboratory equipment and instrumentation, such that testing 'on the spot' cannot normally be carried out. Therefore, there is a need for a method of collecting saliva and processing the saliva once collected that can be performed at the site of collection, for direct use in a diagnostic assay.

The invention provides a device for the collection of saliva from the oral cavity, comprising a mass of saliva absorbing fibrous material having substantially no binding affinity for organic material contained in absorbed saliva, such that expression of saliva from the mass results in substantially all of the protein material being recoverable therefrom.

By organic material herein is meant *inter alia* enzymes, hormones, including protein hormones, proteins generally, including and especially immunoglobulins, vitamins and other low or high molecular weight compounds, including drugs.

An especially suitable fibrous material for use in the saliva collection device according to the invention is rayon. Other suitable materials include the synthetic material sold under the Trade Mark DACRON.

The use of rayon or other fibrous materials having substantially no affinity for organic material contained in saliva is especially advantageous in the case of protein, because it eliminates a common problem observed with such organic materials which is non-specific binding.

Thus, using a rayon absorbent pad or other material with a very low binding capacity for immunoglobulins obviates the need for the addition of agents to the absorbent material to prevent non-specific binding, which agents can cause problems for the patient when the saliva collection pad is inserted in the oral cavity. Furthermore, the use of such agents can lead to problems as regards obtaining regulatory approval for a saliva collection device.

It has been found that rayon material has a high absorption capacity.

The fibrous material for use in the collection of saliva according to the invention can be presented in many forms and shapes.

Thus, the saliva can be collected by means of a pad of the fibrous material. In use, the absorbent pad is wiped over a surface in the oral cavity. The absorbent pad is suitably 1-3 cm in length and 0.5-1.5 cm in diameter and allows for the collection of between 0.1-1.1 ml of saliva when used to collect saliva in accordance with the invention.

An absorbent pad when such is used to collect saliva in accordance with the invention can be mounted at the end of a handle to facilitate the collection of saliva and the transfer thereof, once collected, to the receptacle. Indeed, the absorbent pad and associated handle can resemble a device commonly used in the home and referred to as a cotton bud or tip or as sold under the Trade Mark Q-TIP.

The handle suitably has a length of 6-10 cm and a diameter of 1-3 mm.

The handle is preferably provided with a weakened line adjacent the absorbent pad which facilitates detachment of the handle once the absorbent pad has been inserted in the receptacle for recovery of the collected saliva. Once the pad has been inserted in the receptacle, the handle is broken at the weakened line through a snapping action. More specifically, the absorbent pad is inserted into the receptacle until the

weakened line of the handle lines up with the top edge of the receptacle, the top edge providing resistance for said handle. Once the handle is detached, leaving the pad inside the receptacle, the handle is discarded.

Alternatively, the fibrous material can be presented as a ball which is inserted and retained in the mouth for a given period, followed by collection in a receptacle of a saliva recovery device hereinafter described.

The fibrous material is most suitably spherical or ovoid in shape for ease of use.

However, it will be appreciated that the mass of saliva absorbing material can be of any suitable shape which permits the collection of saliva, when the shaped mass is wiped over a surface in the oral cavity such as the gums or under the tongue for approximately 2 minutes. At the end of the collection period, the saliva impregnated mass or pad is removed from the mouth and transferred to the receptacle for processing of the saliva.

The invention also provides a device for the recovery of saliva from an absorbent, compressible saliva collection device, comprising a receptacle for the saliva collection device and means for compressing the saliva collection device to express saliva and entrained organic material therefrom and to cause egress of the expressed saliva and entrained organic material or a portion thereof from the receptacle.

The device for the recovery of saliva according to the invention enables one to obtain a saliva sample suitable for use in an 'on the spot', rapid immunoassay with a minimum of sample manipulation following collection thereof.

In one embodiment, the walls of the receptacle are flexible and allow for compression of the saliva collection device.

In an alternative embodiment, the receptacle is provided with a piston arrangement for compression of the saliva collection device.

Suitably, the receptacle and piston arrangement are provided with co-operating threaded portions, such that the saliva and entrained material is expressed by screwing the piston into the receptacle.

Preferably, the receptacle is cylindrical in shape, with an open end for inserting the saliva collection device and a closed end having an aperture for expression of the saliva. The piston arrangement is inserted through the open end in use and compresses the saliva collection device towards the closed end.

Further, preferably, the diameter of the cross section of the cylinder increases stepwise at some point along the axis of the receptacle from the closed end to the open end thereof. The stepwise increase may be an abrupt increase or an angled or curved increase. The stepwise increase results in the cylinder having a variable cross-section along its length. The piston arrangement has a cylindrical shape such that the leading end of the piston is a snug fit in the interior of the receptacle at the narrowest part thereof; a threaded portion of the piston arrangement cooperates with a complementary threaded portion provided on the interior of the receptacle at the widest part thereof.

Since the piston arrangement operates by converting the torque due to screwing the parts together into a compressive force at the leading end, a greater efficiency is achieved by reducing the area of the leading end, since the pressure exerted, with a constant force, is inversely proportional to the area over which the force acts.

Suitably, the piston arrangement and the receptacle are provided with roughened areas on their exterior surfaces to assist in screwing and unscrewing the parts. The roughened areas may, for example, be serrated, knurled, rippled or studded. Alternatively, the exterior shapes of the parts may be shaped to assist in twisting the parts relative to one another. An example of this would be where the receptacle,

having a circular interior cross-section, has a hexagonal exterior cross-section; and the piston arrangement has two wings on the end opposite to the leading end, thereby allowing the user to grip and twist the piston arrangement while holding the receptacle tightly.

The threaded portions can each be raised or, alternatively, one threaded portion can be raised and the other sunk on or in the relevant surface, as appropriate.

The piston arrangement can be provided at its leading end with a sealing flange.

Alternatively, the piston arrangement can be provided at its leading edge with a sealing annular ring or O-ring.

Both of the abovementioned alternatives serve to prevent backflow of saliva along the piston arrangement from the leading end thereof.

Furthermore, means can be provided to maintain the compressible saliva collection device and the point of egress of expressed saliva in spaced-apart relationship.

Preferably, the egress of expressed material takes place through a dropper mechanism associated with the receptacle.

Alternatively, the egress of expressed material takes place through a dropper mechanism integral with the receptacle.

Suitably, the dropper mechanism is provided with a filter.

A suitable type of filter is one which comprises one or more layers of a filter material having a gradation of pore sizes in the range 0.5-5 μm.

Further, preferably, the final layer through which the material percolates should have a pore size no greater than 1.0 μm.

Suitable materials for use in the filtration device include layers of glass, ceramic, wood, paper, etc., more especially glass.

With such an arrangement, filtrate can be transferred in droplets of a predetermined size, when desired.

The device for the recovery of saliva in accordance with the invention can be a device of the type disclosed in our Patent No. S58662, wherein the walls of the receptacle are flexible, but which does not necessitate the use of a buffer for facilitating the release of the analyte of interest from the mass of absorbent material. In accordance with the invention, the use of a buffer is optional. The saliva and entrained material are trapped in the fibres of the absorbent fibrous material according to the invention and are released upon squeezing, without the requirement for a releasing agent which would be required in the case of bound material. When a buffer is used the mass of absorbent material is inserted into the receptacle, which suitably has a tubular shape approximately 3 cm in length and with a diameter of 1.5 cm, resulting in saturation of the absorbent material by the buffer. By squeezing the receptacle several times, the antibodies will equilibrate with the buffer. Suitably, the receptacle contains approximately 0.75 ml of phosphate buffered saline (PBS).

If the receptacle is provided with a dropper mechanism with an integral filter of the type disclosed in our Patent No. S58662, the receptacle is inverted with the filtration device mounted at the free end and organic material such as immunoglobulin material, free of mucous, tissue and food debris resulting from the filtration process is obtained in a form ready to use in an immunoassay.

A dropper mechanism when used in association with the filtration device suitably provides drops of processed liquid of approximately 30-70 μl.

In such a device, the flexible receptacle is preferably formed of a flexible plastics material.

The receptacle can also suitably be provided with a cap or other closing means.

The device for the recovery of saliva in accordance with the invention is suitably integral with an assay card for the detection of an analyte by bi-directional lateral chromatography. Assay card systems for the detection of an analyte by bi-directional lateral chromatography are the subject of U.S. Patent No. 5,006,474.

Alternatively, the device for the recovery of saliva in accordance with the invention is suitably integral with an assay card for the detection of an analyte by sequential activation of immobilized reagents. Such systems for the detection of an analyte by sequential activation of immobilised reagents are the subject of International Patent Publication WO 88/08534.

When the device for the recovery of saliva is of the type which is provided with a piston arrangement, the piston suitably has a hollow interior in which the saliva collection device can be stored prior to use. The hollow interior may be open or it may be sealed with a snap-off cap which is removed prior to use. The snap-off cap portion is suitably made of polyethylene.

The invention also provides a kit-of-parts comprising a device for the collection of saliva as hereinabove described and a device for the recovery of saliva as hereinabove described. Such a kit-of-parts provides apparatus which allows one to collect saliva from the oral cavity in sufficient amounts and in a form for direct use in an immunoassay, without a requirement for the usual laboratory instrumentation for the recovery and any processing of the saliva once collected, as herein described.

Saliva collected and recovered with the apparatus in accordance with the invention can be assayed by conventional methods with or without modifications, as required. Such modifications are minor. For example, a slightly more concentrated enzyme conjugate reagent may be required than would be used in a corresponding assay carried out on blood. Other modifications involve the use of an increased volume of saliva relative to serum, a decreased diluent volume and a lowering of the optical density cutoff to 70% of the serum value (see Frerichs R.R., *et al.* (1992) The Lancet, Vol. 340, Dec. 19/26, 1496-1499).

The Ig levels recovered are found to be high enough to be detectable by currently available assays. For example, many of the standard kits for testing HIV in serum can, with minor adjustments, be used for HIV testing on saliva. Such assays include Abbott HIVAB HIV-1 EIA and Abbott TestPack HIV-1 HIV-2 Kit (Abbott Laboratories Inc.) and HIV-1 Western Blot Kit (Biotech/Du Pont).

It will be appreciated that the basic assay will normally be an enzyme immunoassay.

The invention will be further illustrated by the following description of embodiments thereof given by way of example only with reference to the accompanying drawings in which: -

Fig. 1 is an exploded schematic representation of a first embodiment of a device according to the invention for the recovery of saliva from an absorbent, compressible saliva collection device;

Fig. 2 is an exploded schematic representation of a second embodiment of a device according to the invention for the recovery of saliva from an absorbent, compressible saliva collection device;

Fig. 3 is a schematic representation of a device according to the invention for collection of saliva;

Fig. 4 is an exploded schematic representation of a third embodiment of a device according to the invention for the recovery of saliva from an absorbent, compressible saliva collection device;

Fig. 5 is a plan view of one part of the device of Fig. 4; and

Fig. 6 is an exploded schematic representation of a fourth embodiment of a device according to the invention for the recovery of saliva from an absorbent, compressible saliva collection device.

Referring to Fig. 1, there is indicated generally at 10, a device for the recovery of saliva from an absorbent compressible ball of rayon fibres (not shown), which has been used to collect saliva in the manner hereinabove described. The device 10 is in two parts, namely a receptacle 11 in which the rayon ball is inserted following saliva collection and part 12 receivable in the receptacle 11. The receptacle 11 has at least a partial circumferentially extending thread 13 on its inner surface which is engageable with a cooperating thread 14 on the part 12. The receptacle 11 is provided with a dropper mechanism 15 at its end 16 remote from the open end 17. The rayon ball, which has been used to collect saliva, is inserted in the receptacle 11 and then the part 12 is screwed into the receptacle 11 so as to compress the ball to express the collected saliva, which in turn is expressed through the dropper mechanism 15 for use in an immunoassay.

Part 12 has a hollow interior 18 within which the rayon ball can be accommodated prior to use.

Referring to Fig. 2, there is indicated generally at 20, a device for the processing of collected saliva. The device 20 comprises a tubular receptacle 21, 3 cm long and 1.5 cm in diameter and is made of a flexible plastics material. The receptacle 21 receives at its open end 22, a filtration device 23 with an integral dropper mechanism 24. The filtration device 23 can be inter-engageable with the receptacle 21 in

known manner and in such a way that the device is sealed against any egress of the sample when the device 20 is in an inverted mode, other than through the filtration device 23 and the associated dropper mechanism 24. The filtration device 23 in the engaged position abuts an internal rib 25 provided on the receptacle 21.

Referring to Fig. 3, there is indicated generally at 26, a saliva collection device having an absorbent pad 27 of rayon material mounted on a plastics handle 28. The absorbent pad 27 is 1.5 cm long and 1.0 cm in diameter. The handle 28 is 6 cm long is provided with a weakened line 29 adjacent the absorbent pad 27.

In use, the device 26 is used to collect a sample of saliva on the absorbent pad 27 from the oral cavity of a patient as hereinabove described.

The device 26 is used to transfer a collected sample to the device 20 which contains an amount of a buffer such as PBS, suitably 0.75 ml, at pH 7.2. The device 26 is inserted into the receptacle 21 to an extent such that the weakened line 29 is adjacent the upper edge thereof, whereupon the handle 28 is broken off by a snapping action and discarded. The filtration device 23 and integral dropper mechanism 24 is attached to the device 20 and the walls of the device 20 are squeezed so as to facilitate release of bound antibody into the PBS buffer. The device 20 is then inverted, whereupon the contents of the device percolate through filtration device 23, assisted by further squeezing of the tubular body 21. The filtration device 23 has a number of layers of a filter material (not shown) as hereinabove described with graded pore sizes which retain mucous, tissue and food debris contained in saliva while permitting immunoglobulins to pass therethrough into the dropper mechanism 24 for collection. Droplets of filtrate are collected from the dropper mechanism 24 for use in an immunoassay.

Referring to Fig. 4, there is indicated generally at 30, a device for the recovery of saliva from an absorbent compressible ball of rayon fibres (not shown), which has been used to collect saliva in the

manner hereinabove described. The device is in two parts, namely a receptacle 31 in which the rayon ball is inserted following saliva collection and part 32, which is a piston arrangement, receivable in the receptacle 31. The receptacle 31 has at least a partial circumferentially extending thread 33 on its inner surface which is engageable with a cooperating thread 34 on the part 32. A circumferentially extending sealing flange 35 is provided at the leading end 36 of part 32. The receptacle 31 is provided with a dropper mechanism 37 at its end 38 remote from the open end 39. The rayon ball, which has been used to collect saliva, is inserted in the receptacle 31 and then the part 32 is screwed into the receptacle 31 so as to compress the ball to express the collected saliva, which is then expressed through the dropper mechanism 37 for use in an immunoassay. The sealing flange 35 co-operates with the wall 40 of receptacle 31, in use, to assist in preventing backwise flow of the saliva towards the open end 39.

Referring to Fig. 5, there is shown a plan view of the receptacle 31 shown in Fig. 4. A plurality of raised ridges 41 extend across the inner surface 42 of the end 38. The ridges 41 prevent the possibility of the dropper mechanism 37 becoming blocked by the compressed rayon ball in use.

Referring to Fig. 6, there is indicated generally at 50, a device for the recovery of saliva similar to the device of Fig. 4. The device 50 has a receptacle 51 with a substantially cylindrical form, the diameter of which increases stepwise between end 52, having an integral dropper mechanism 53, and open end 54. The stepwise increase in diameter occurs over a short region which has the form of an angled slope 55.

A piston arrangement 56 has a cylindrical shape suitable to snugly fit the interior of the receptacle 51, and leading end 57 of the piston arrangement 56 is provided with a nitrile O-ring 58 which ensures a tight seal between the leading end 57 of the piston arrangement 56 and the receptacle 51. The piston arrangement 56 has

a raised thread 59 complementary to a sunken thread 60 in the interior of the receptacle 51.

Both the receptacle 51 and the piston arrangement 56 are provided with roughened areas 61,62 on their exterior surfaces which assist in screwing and unscrewing the receptacle parts. The roughened areas 61,62 are serrations moulded into the receptacle 51 and piston arrangement 56, respectively.

The piston arrangement 56 is provided with a compartment 63 which is adapted to store a rayon ball 64 before use. The compartment is hygenically sealable with a snap-fit polyethylene cap 65 provided with a protruding tab 66 which facilitates the removal of the cap 65.

* * * *

Example

Saliva was collected from 25 HIV positive patients and 5 HIV negative controls using a rayon saliva collection device according to the invention. The saliva samples collected were tested for HIV using the SalivaCard (SalivaCard is a Trade Mark) HIV 1/2 test (Trinity Biotech Plc, Dublin, Ireland). Anti-HIV antibodies were detected in the saliva of all 25 HIV positive patients and no non-specific antibody was detected in the 5 negative controls.

* * * *

The apparatus according to the invention is particularly suitable for use by hospital emergency rooms, clinics, medical and dental surgeries, and additionally in settings where HIV testing has become routine, such as in screening armed forces personnel, prisoners, insurance applications and for assessing immigrants.

Claims

1. A device for the collection of saliva from the oral cavity, comprising a mass of saliva absorbing fibrous material having substantially no binding affinity for organic material contained in absorbed saliva, such that expression of saliva from the mass results in substantially all of the protein material being recoverable therefrom.

2. A device for the recovery of saliva from an absorbent, compressible saliva collection device, comprising a receptacle for the saliva collection device and means for compressing the saliva collection device to express saliva and entrained organic material therefrom and to cause egress of the expressed saliva and entrained organic material or a portion thereof from the receptacle.

3. A device according to Claim 2, wherein the device is provided with a piston arrangement for compression of the saliva collection device, and wherein the receptacle and piston arrangement are provided with co-operating threaded portions, such that the saliva and entrained material is expressed by screwing the piston into the receptacle.

4. A kit-of-parts comprising a device according to Claim 1 for the collection of saliva and a device for the recovery of saliva according to Claim 2 or 3.

5. A kit-of-parts according to Claim 4, substantially as hereinbefore described with particular reference to the accompanying drawings.

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Agents for the Applicants.

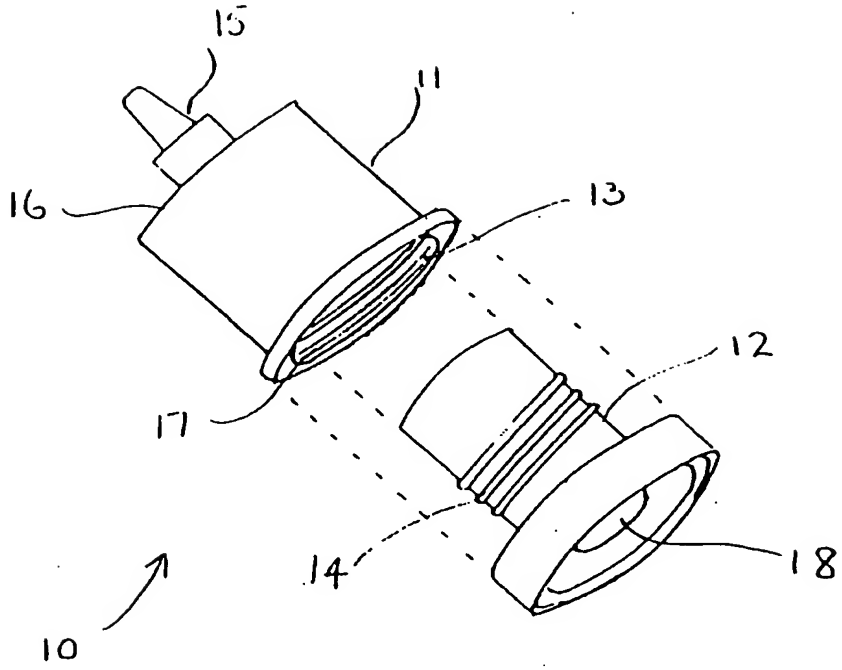

FIG. 1

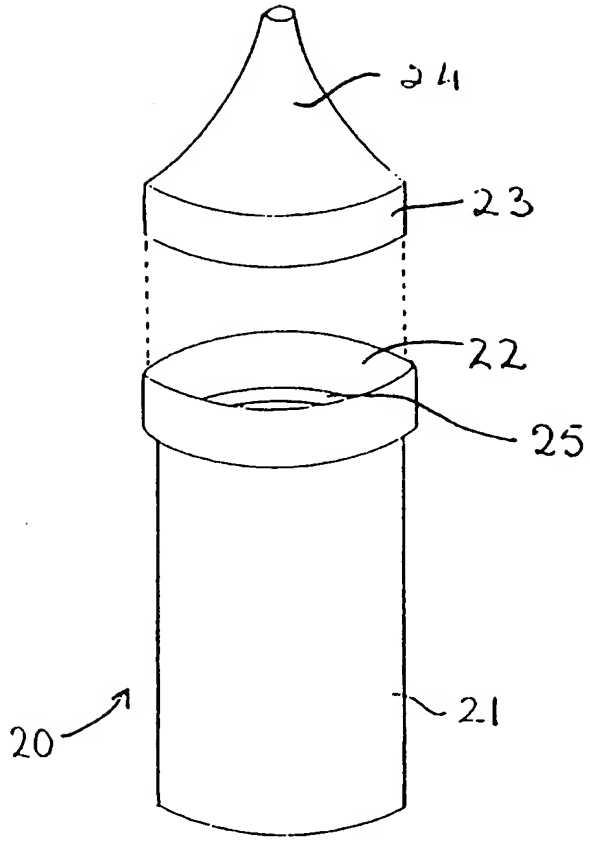

FIG. 2

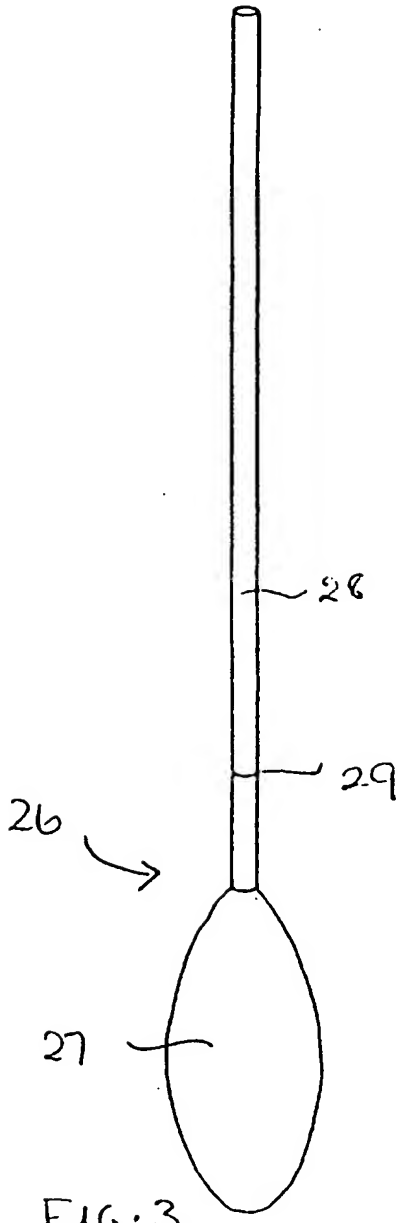

FIG. 3

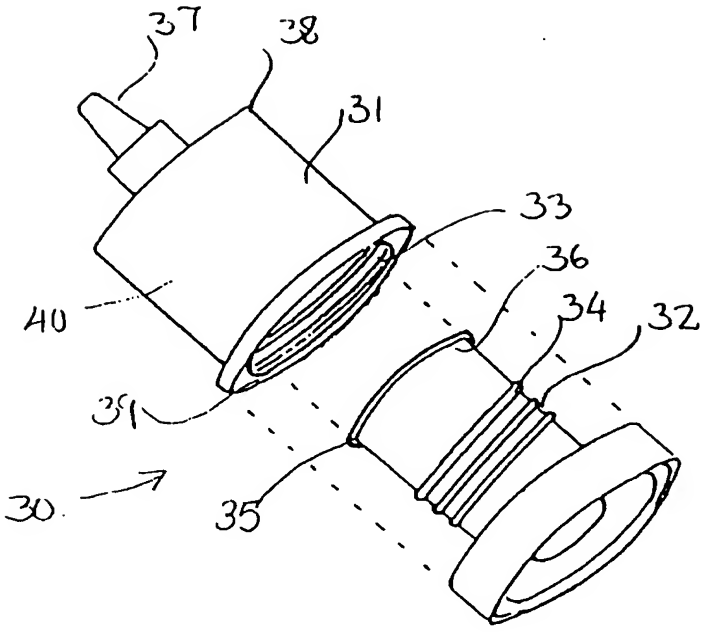

FIG 4

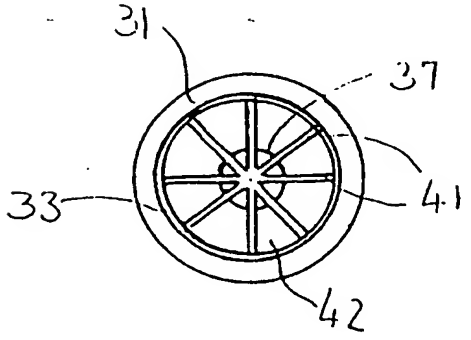

FIG. 5

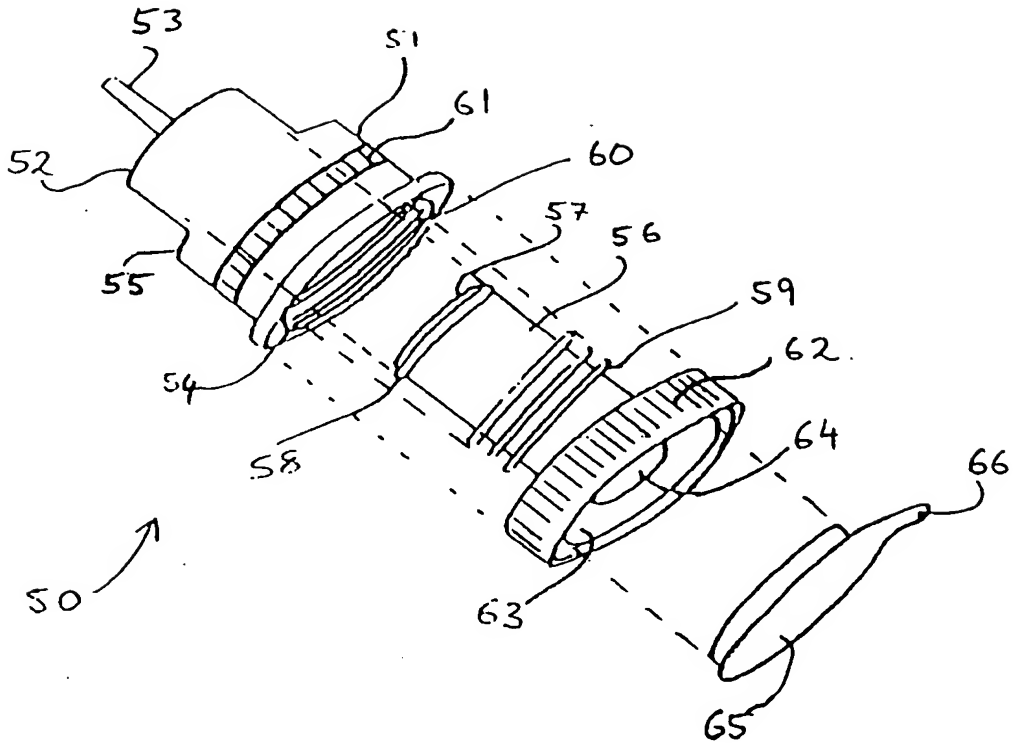

FIG. 6